

FIGURE 1

66220T" 9T552460

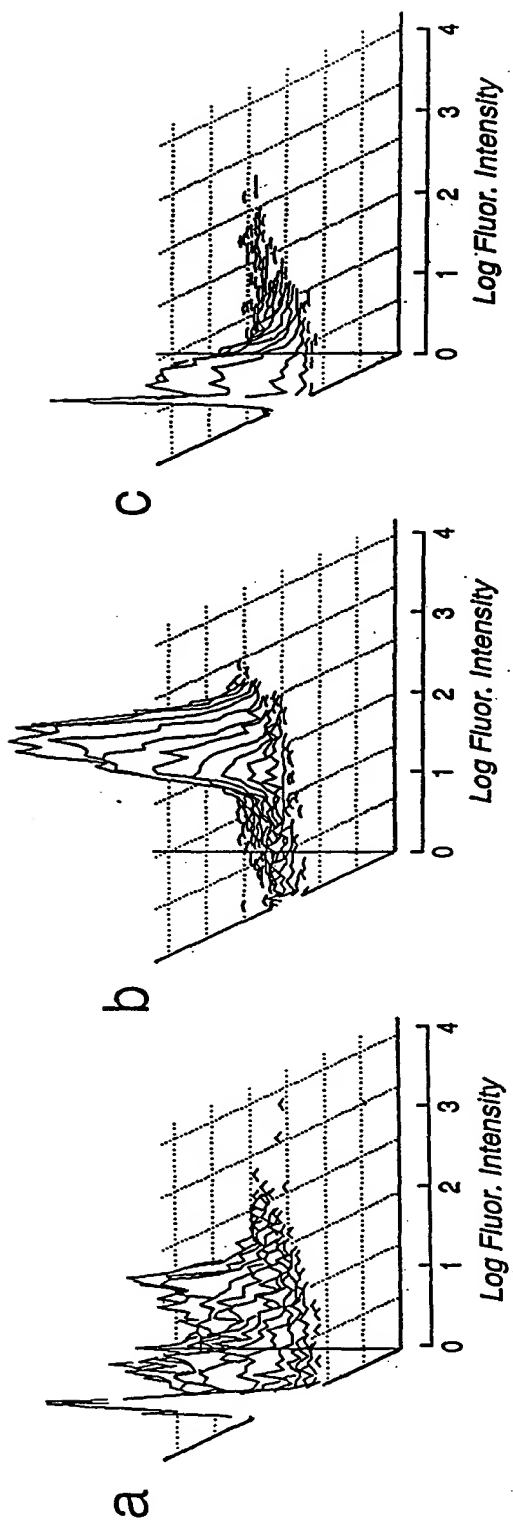


FIGURE 2

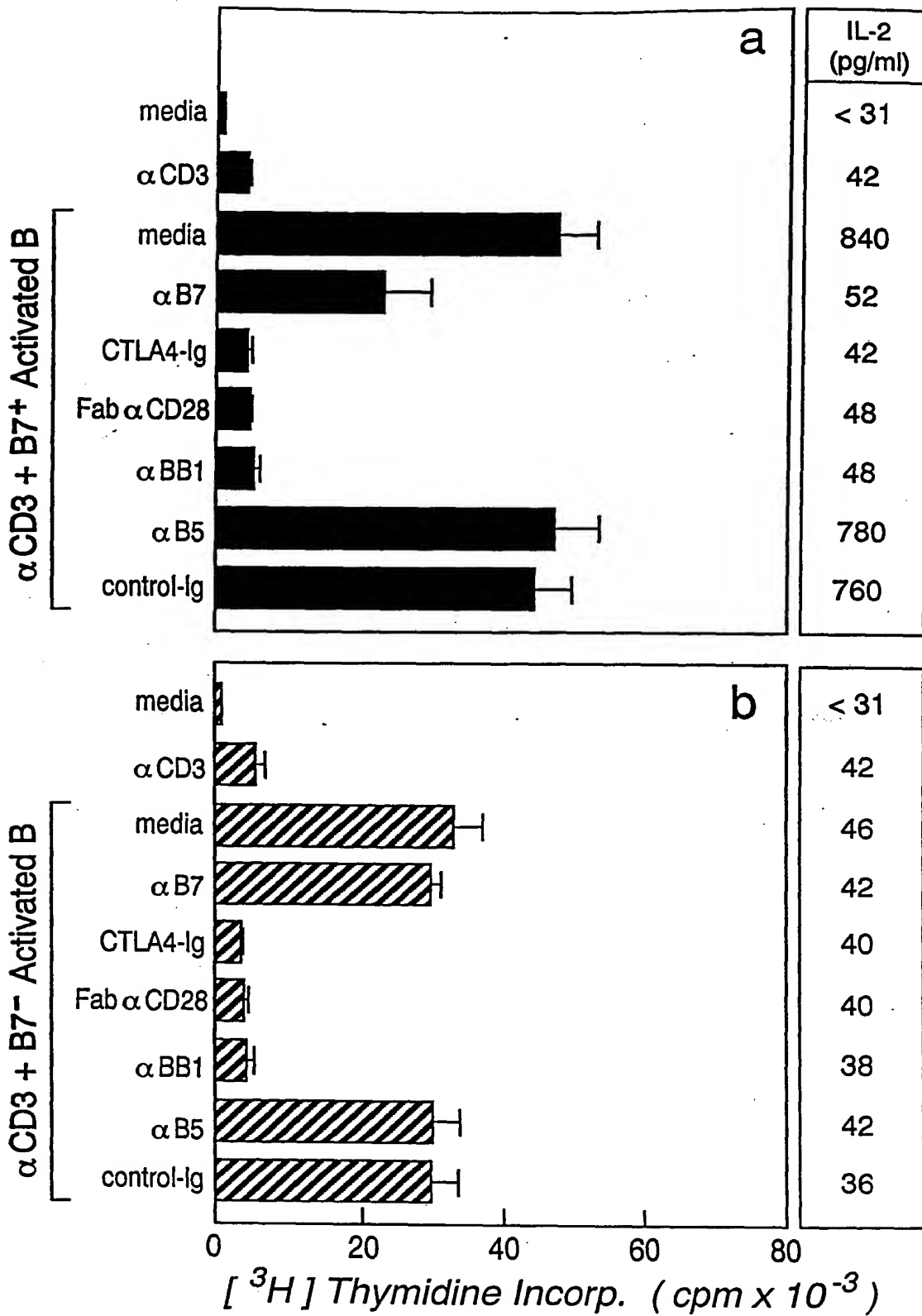


FIGURE 3

652201" 9T552460

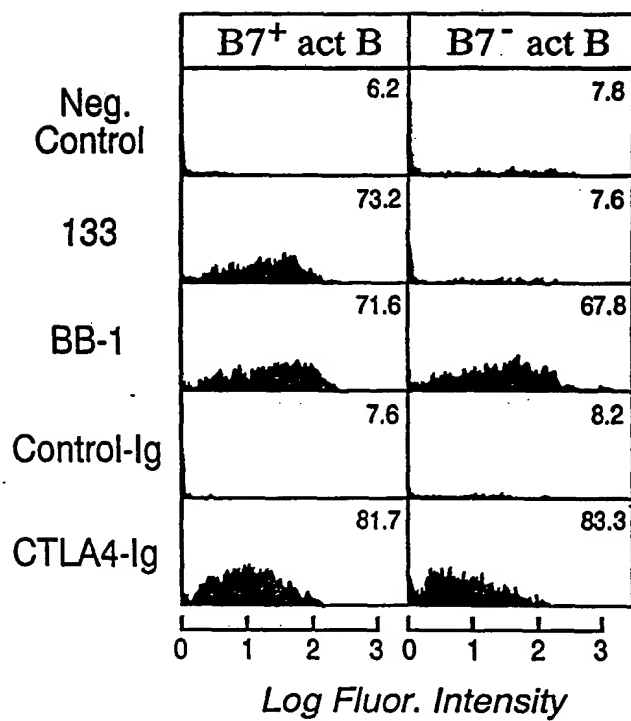


FIGURE 4

# B Cells Activated by sIg Crosslinking

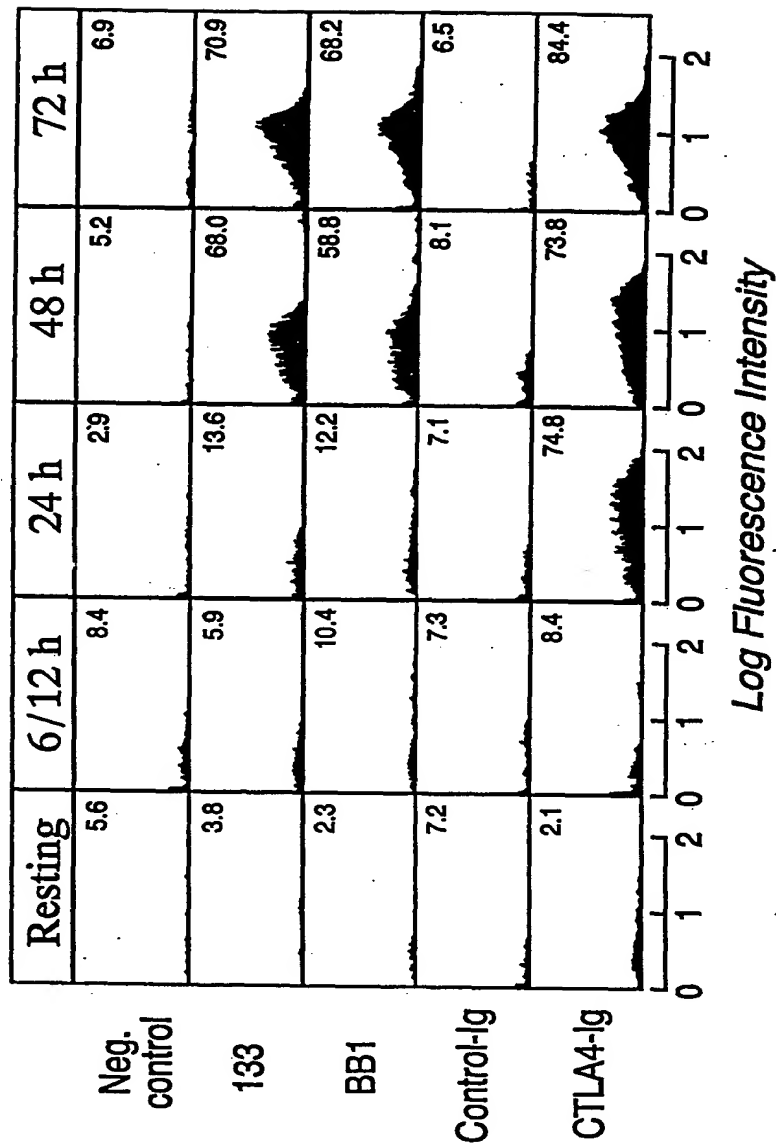


FIGURE 5

# B Cells Activated by Class II Crosslinking

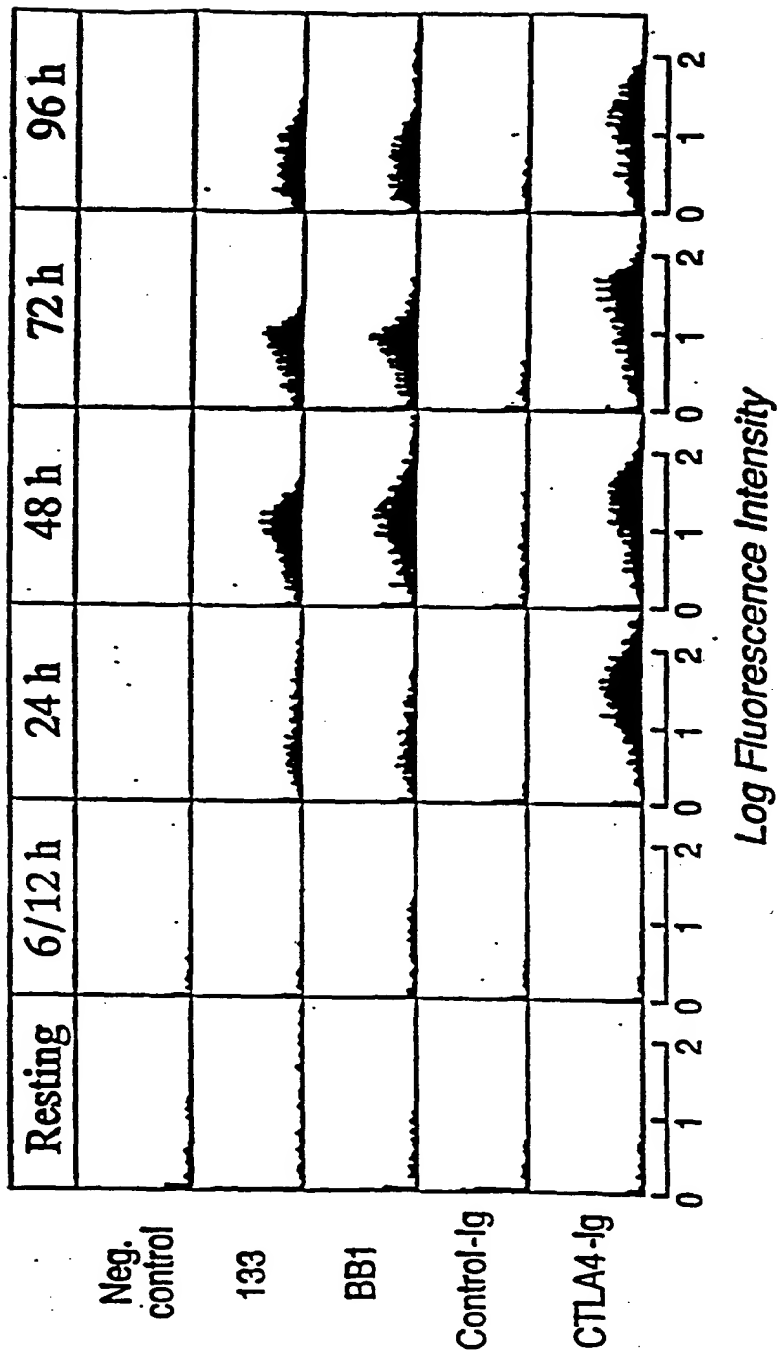


FIGURE 6

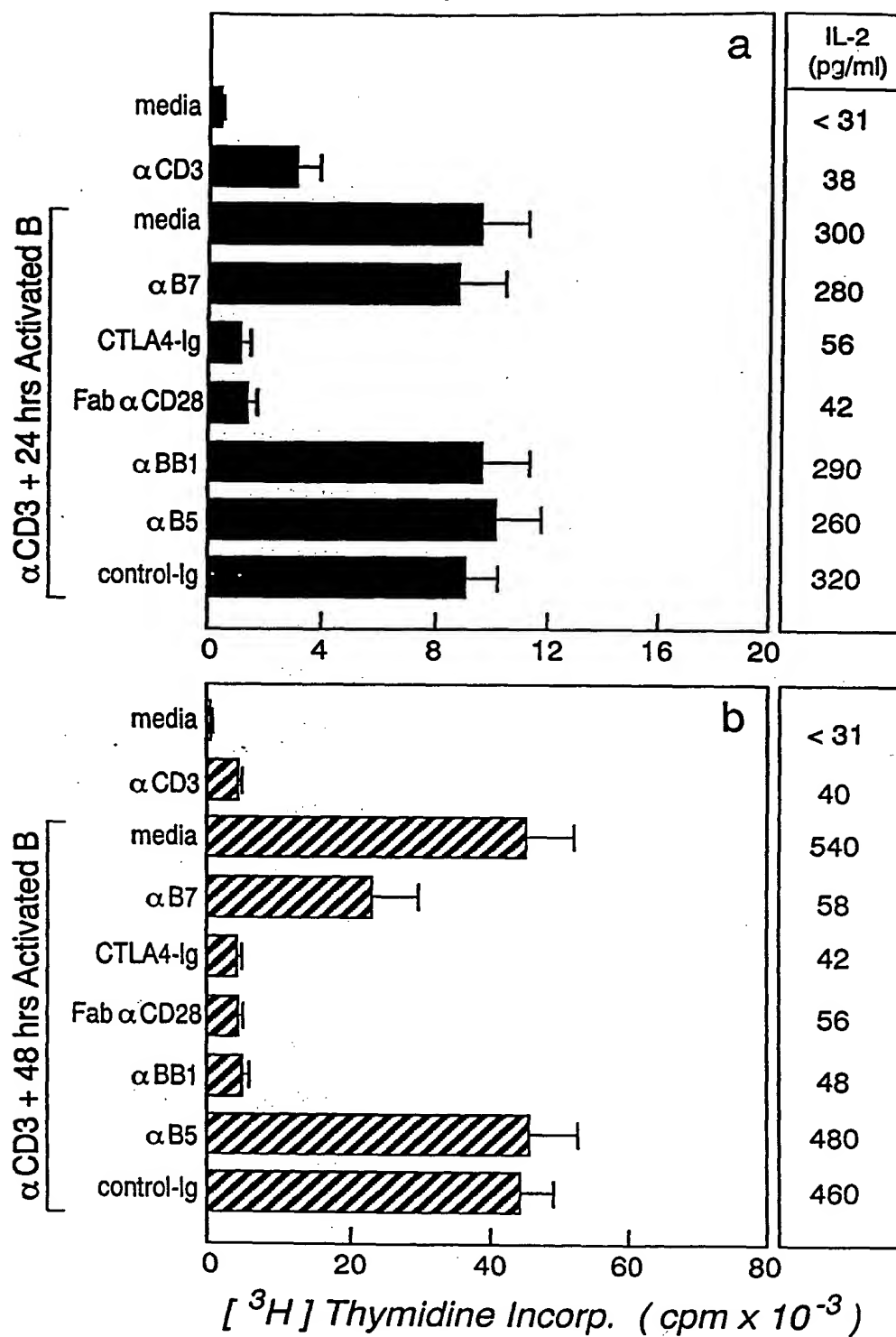


FIGURE 7

1 CACAGGGTGAAAGCTTTGCTTCTCTGCTGCTGTAACAGGGACTAGCACAGACACACGGATGAGTGGGGTC 70  
 71 ATTTCCAGATATTAGGTCACAGCAGAAGCAGCCAAAATGGATCCCCAGTGCACTATGGGACTGAGTAACA 140  
 M D P Q C T M G L S N 11  
 141 TTCTCTTTGTGATGGCCTTCCTGCTCTCTGGTGTCTCCTCTGAAGATTCAAGCTTATTTCAATGAGAC 210  
 12 I L F V M A F L L S G A A P L K I Q A Y F N E T 35  
 #  
 211 TGCAGACCTGCCATGCCAATTTGCAAACCTCTCAAAACCAAAGCCTGAGTGAGCTAGTAGTATTTTGGCAG 280  
 36 A D L P C Q F A N S Q N Q S L S E L V V F W Q 58  
 \* #  
 281 GACCAGGAAAACCTTGGTTCTGAATGAGGTATACTTAGGCAAAGAGAAATTTGACAGTGTTCATTCCAAGT 350  
 59 D Q E N L V L N E V Y L G K E K F D S V H S K 81  
 351 ATATGGGCCCGCACAAAGTTTTGATTCCGGACAGTTGGACCCTGAGACTTCACAATCTTCAGATCAAGGACAA 420  
 82 Y M G R T S F D S D S W T L R L H N L Q I K D K 105  
 421 GGGCTTGATCAATGTATCATCCATCACAAAAAGCCACAGGAATGATTGCGATCCACCAGATGAATTCT 490  
 106 G L Y Q C I I H H K K P T G M I R I H Q M N S 128  
 \*  
 491 GAACTGTCAGTGCTTGCTAACTTCAGTCAACCTGAAATAGTACCAATTTCTAATATAACAGAAAAATGTGT 560  
 129 E L S V L A N F S Q P E I V P I S N I T E N V 151  
 # #  
 561 ACATAAATTTGACCTGCTCATCTATACACGGTTACCCAGAACCTAAGAAGATGAGTGTTTGTCTAAGAAC 630  
 152 Y I N L T C S S I H G Y P E P K K M S V L L R T 175  
 # \*  
 631 CAAGAATTCAACTATCGAGTATGATGGTATTATGCAGAAATCTCAAGATAATGTCACAGAACTGTACGAC 700  
 176 K N S T I E Y D G I M Q K S Q D N V T E L Y D 198  
 # #  
 701 GTTTCATCAGCTTGTCTGTTTCATTCCCTGATGTTACGAGCAATATGACCATCTTCTGTATTCTGGAAA 770  
 199 V S I S L S V S F P D V T S N M T I F C I L E 221  
 # \*  
 771 CTGACAAGACGCGGCTTTTATCTTCACCTTTCTCTATAGAGCTTGAGGACCCTCAGCCTCCCCCAGACCA 840  
 222 T D K T R L L S S P F S I E L E D P Q P P P D H 245

FIGURE 8A



841	CATTCCTTGGATTACAGCTGTACATCCAACAGTTATTATATGTGTGATGGTTTTCTGTCTAATTCTATGG	910
246	<u>I P W I T A V L P T V I I C V M V F C L I L H</u>	268
911	AAATGGAAGAAGAAGAAGCGGCCTCGCAACTCTTATAAATGTGGAACCAACACAATGGAGAGGGAAGAGA	980
269	K W K K K K R P R N S Y K C G T N T M E R E E	291
981	GTGAACAGACCAAGAAAAGAGAAAAAATCCATATACCTGAAAGATCTGATGAAGCCCAGCGTGTTTTTAA	1050
292	S E Q T K K R E K I H I P E R S D E A Q R V F K	315
1051	AAGTTCGAAGACATCTTCATGCGACAAAAGTGATACATGTTTTTAATTAAAGAGTAAAGCCCCAAAAAAA	1120
316	S S K T S S C D K S D T C F *	329

FIGURE 8 B

09425516 102239

0925516-10239  
652201-9155260

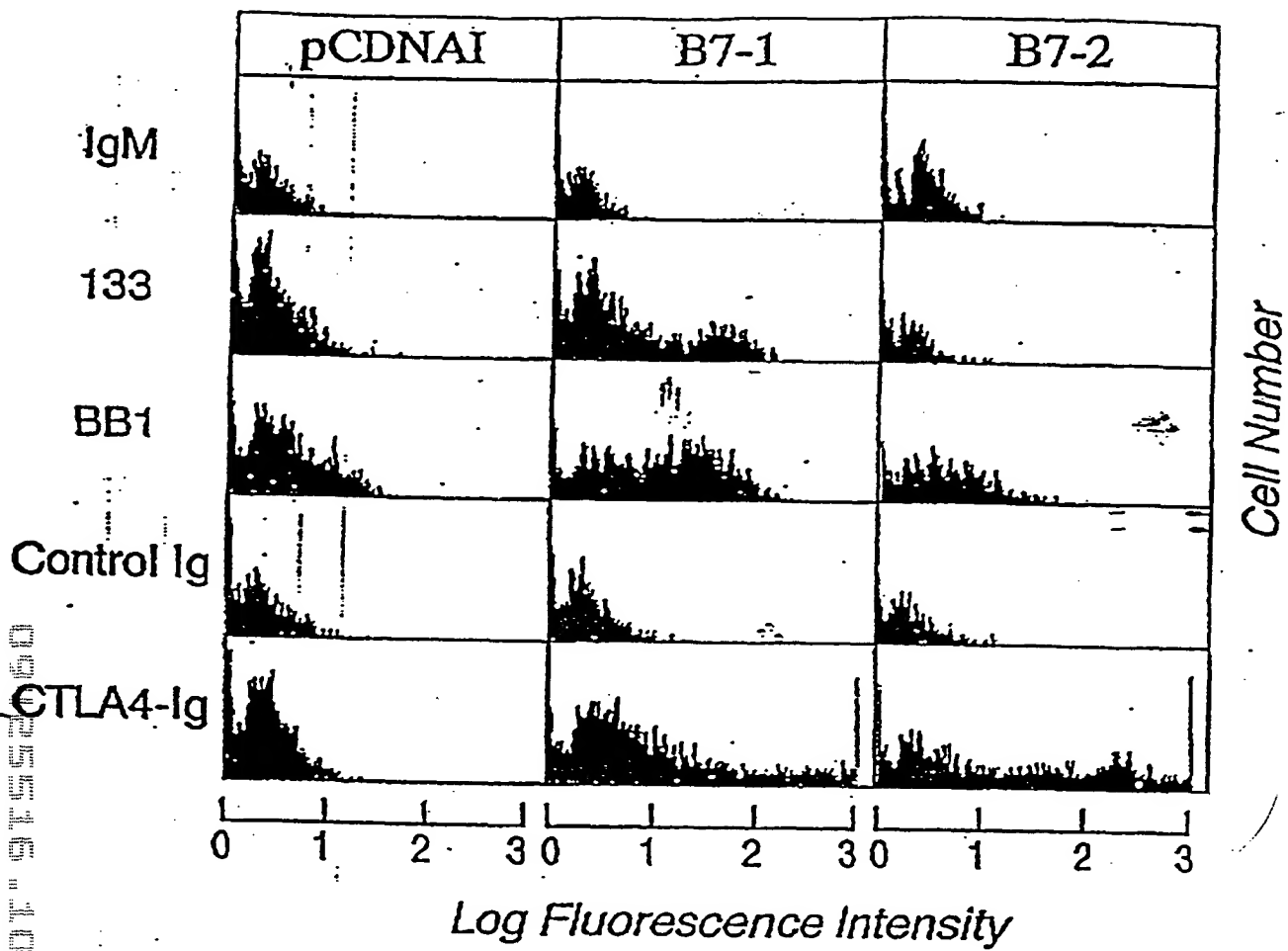
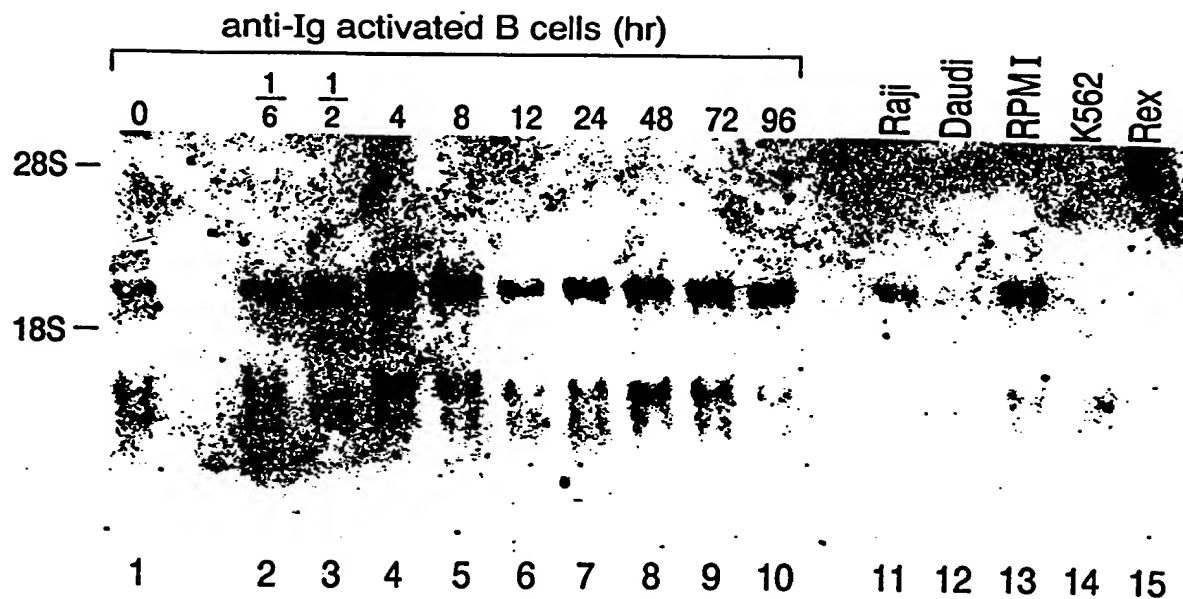
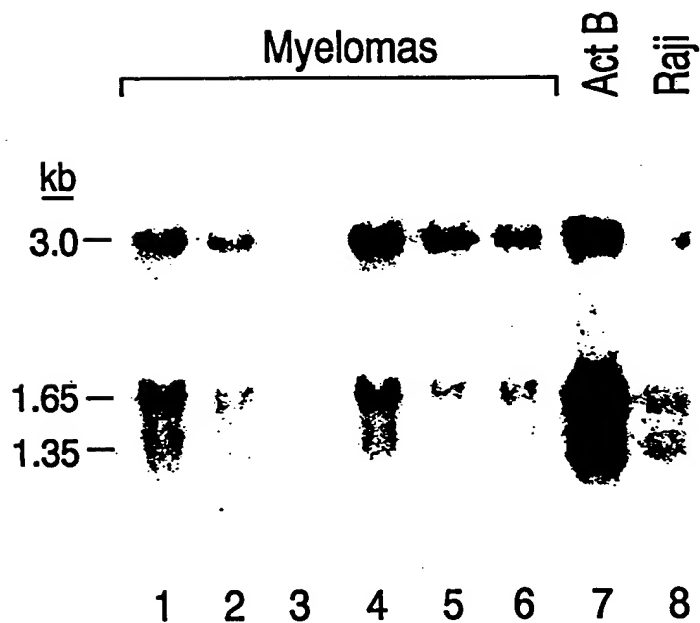


FIGURE 9



panel a



panel b

FIGURE 10

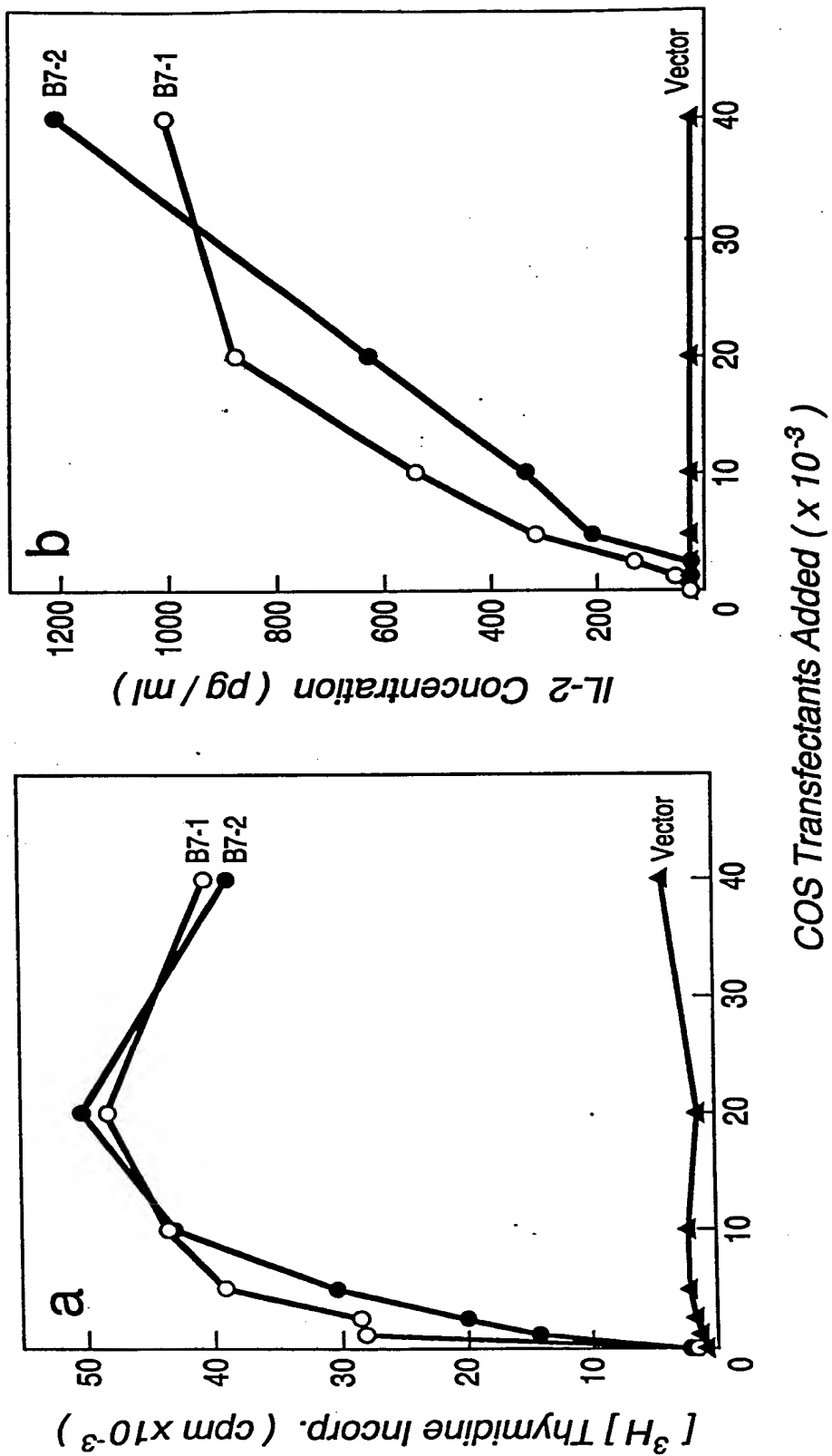
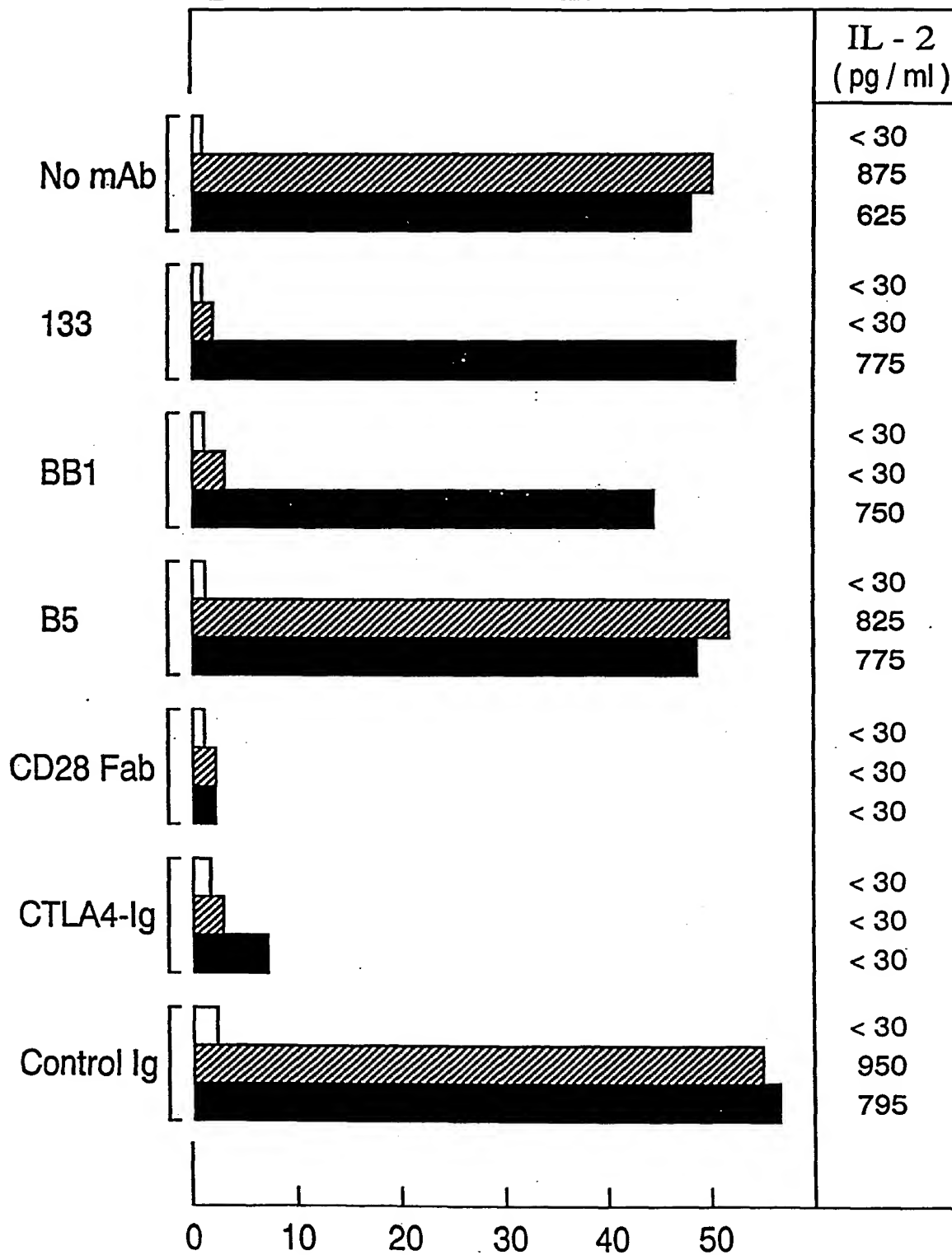


FIGURE 11

CD28<sup>+</sup> T cells + PMA :

□ Vector    ▨ B7-1    ■ B7-2



[<sup>3</sup>H] Thymidine Incorpor. (cpm x 10<sup>-3</sup>)

FIGURE 12

hB7-1	1	M..GHTRRQGTSPSKCPYLNFFQLLV.LAGLSHFCSGV.IHVTKEVKEVA	46
hB7-2	1	M.....DPOCTMGLSN.....ILFVMAFLLSGA...APLKIQAYFNETA	36
mB7	1	MACNCQLMQDTPLLKFPCPRLILLFVLLIRLSQVSSDVDEQLSKSVKDKV	50
hB7-1	47	TLSCGHNVSVEE.LAQTRIWQKEKKMVL.T.MMSGDMNI...WPEYKNRT	91
hB7-2	37	DLPCQFANSQNSLSLVVFWQDQENLVLNEVYLGKEKFDSVHSKYMGRT	86
mB7	51	LLPCRY.NSPHEDESEDRIYWQKHDKVLS.VIAGKLV...WPEYKNRT	95
hB7-1	92	IFDITNNLSIVILALRPSDEGTYECVVLKYEKDAFKREHLAEVTL SVKAD	141
hB7-2	87	SFD.SDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSLSVLN	135
mB7	96	LYDNTT.YSLIILGLVLSDRGTYSVVQKKERGTYEVKHLALVKL SIKAD	144
hB7-1	142	FPTPSISDFEIPTSNI.RRIICSTSGGFPEPH....LSWLENGEELNAIN	186
hB7-2	136	FSQPEIVPISNITENVYINLTCSIIHGYPEPKKMSVLLRTKNSTIEYDGI	185
mB7	145	FSTPNITESGNPSADT.KRITCFASGGFPKPR....FSWLENGRELPGIN	189
hB7-1	187	TTVSQDPETELYAVSSKLDN...MTTNHSFMCLIKYGHLRVNQTFNWNT	233
hB7-2	186	MQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETDKTRLLSSPFSIE	235
mB7	190	TTISQDPESELYTISSQLDN...TTRNHTIKCLIKYGDAHVSEDFTWEK	236
hB7-1	234	TKQEHF.PDNLLPSWAITLISVNGIFVICCLTYCFAPRCRERRRNERLRR	282
hB7-2	236	.LEDPPPPDHIPWITAVLP....TVIICVMVFCLILWKWKKKKRPRNSY	280
mB7	237	PPEDPPDSKNTLVLFAGFGAVITVVVIVVVIKCFCKHRSCFRNEA.SR	285
hB7-1	283	ESVRPV*	288
hB7-2	281	KCG...TNTMEREESQTKKREKIHIPERSDEAQRVFKSSKTSSCDKSDT	327
mB7	286	ETNNSLTFGPEEALAEQTVFL*	306
hB7-2	328	CG*	329

FIGURE 13

```

CCCACGCGTCCGGGAGCAAGCAGACGCGTAAGAGTGGCTCCTGTAGGCAGCACGGACTTG
1 -----+-----+-----+-----+-----+-----+-----+ 60
GGGTGCGCAGGCCCTCGTTCGTCTGCGCATTCCTACCGAGGACATCCGTCTGCCTGAAC

AACAAACCAGACTCCTGTAGACGTGTTCCAGAACTTACGGAAGCACCCACGATGGACCCCA
61 -----+-----+-----+-----+-----+-----+-----+ 120
TTGTTGGTCTGAGGACATCTGCACAAGGTCTTGAATGCCTTCGTGGGTGCTACCTGGGGT

M D P R -

GATGCACCATGGGCTTGGCAATCCTTATCTTTGTGACAGTCTTGCTGATCTCAGATGCTG
121 -----+-----+-----+-----+-----+-----+-----+ 180
CTACGTGGTACCCGAACCGTTAGGAATAGAAACACTGTCAGAACGACTAGAGTCTACGAC

C T M G L A I L I F V T V L L I S D A V -

TTTCCGTGGAGACGCAAGCTTATTTCAATGGGACTGCATATCTGCCGTGCCCATTTACAA
181 -----+-----+-----+-----+-----+-----+-----+ 240
AAAGGCACCTCTGCGTTTGAATAAAGTTACCTGACGTATAGACGGCACGGGTAAATGTT

S V E T Q A Y F N G T A Y L P C P F T K -

AGGCTCAAAACATAAGCCTGAGTGAGCTGGTAGTATTTTGGCAGGACCAGCAAAAGTTGG
241 -----+-----+-----+-----+-----+-----+-----+ 300
TCCGAGTTTTGTATTTCGGACTCACTCGACCATCATAAAACCGTCTGGTCTGTTTTCAACC

A Q N I S L S E L V V F W Q D Q Q K L V -

TTCTGTACGAGCACTATTTGGGCACAGAGAACTTGATAGTGTGAATGCCAAGTACCTGG
301 -----+-----+-----+-----+-----+-----+-----+ 360
AAGACATGCTCGTGATAAACCCGTGTCTCTTTGAACTATCACACTTACGGTTCATGGACC

L Y E H Y L G T E K L D S V N A K Y L G -

GCCGCACGAGCTTTGACAGGAACAACCTGGACTCTACGACTTCACAATGTTTCAAGTCAAGG
361 -----+-----+-----+-----+-----+-----+-----+ 420
CGGCGTGCTCGAAACTGTCTTGTGACCTGAGATGCTGAAGTGTACAAAGTCTAGTTCC

R T S F D R N N W T L R L H N V Q I K D -

ACATGGGCTCGTATGATTGTTTTATACAAAAAAGCCACCCACAGGATCAATTATCCTCC
421 -----+-----+-----+-----+-----+-----+-----+ 480
TGTACCCGAGCATACTAACAAAATATGTTTTTTTCGGTGGGTGTCCTAGTTAATAGGAGG

M G S Y D C F I Q K K P P T G S I I L Q -

AACAGACATTAACAGAACTGTGAGTATCGCCAACTTCAGTGAACCTGAAATAAACTGG
481 -----+-----+-----+-----+-----+-----+-----+ 540
TTGCTCTGTAATTGTCTTGACAGTCACTAGCGGTTGAAGTCACTTGGACTTTATTTTGACC

Q T L T E L S V I A N F S E P E I K L A -

CTCAGAATGTAACAGGAAATTCTGGCATAAATTTGACCTGCACGTCTAAGCAAGGTCACC
541 -----+-----+-----+-----+-----+-----+-----+ 600
GAGTCTTACATTGTCCTTTAAGACCGTATTTAAACTGGACGTGCAGATTTCGTTCCAGTGG

Q N V T G N S G I N L T C T S K Q G H P -

```

FIGURE 14 A

CGAAACCTAAGAAGATGTATTTTCTGATAACTAATTCAACTAATGAGTATGGTGATAACA  
 601 -----+-----+-----+-----+-----+ 660  
 GCTTTGGATTCTTCTACATAAAAGACTATTGATTAAGTTGATTACTCATACCACCTATTGT  
 K P K K M Y F L I T N S T N E Y G D N M -  
 TGCAGATATCACAAGATAATGTCACAGAACTGTTTCAGTATCTCCAACAGCCTCTCTCTTT  
 661 -----+-----+-----+-----+-----+ 720  
 ACGTCTATAGTGTTCTATTACAGTGCTTTGACAAGTCATAGAGGTTGTCTGGAGAGAGAGAAA  
 Q I S Q D N V T E L F S I S N S L S L S -  
 CATTCCCGGATGGTGTGTGGCATATGACCGTTGTGTGTGTTCTGGAAACGGAGTCAATGA  
 721 -----+-----+-----+-----+-----+ 780  
 GTAAGGGCCTACCACACACCGTATACTGGCAACACACACAAGACCTTTGCCTCAGTTACT  
 F P D G V W H M T V V C V L E T E S M K -  
 AGATTTCTCTCAAACCTCTCAATTTCACTCAAGAGTTTCCATCTCCTCAAACGTATTGGA  
 781 -----+-----+-----+-----+-----+ 840  
 TCTAAAGGAGGTTTGGAGAGTTAAAGTGAGTTCTCAAAGGTAGAGGAGTTTGCATAACCT  
 I S S K P L N F T Q E F P S P Q T Y W K -  
 AGGAGATTACAGCTTCAGTTACTGTGGCCCTCCTCCTTGTGATGCTGCTCATCATTGTAT  
 841 -----+-----+-----+-----+-----+ 900  
 TCCTCTAATGTCTGAAGTCAATGACACCGGGAGGAGGAACACTACGACGAGTAGTAACATA  
 E I T A S V T V A L L L V M L L I I V C -  
 GTCACAAGAAGCCGAATCAGCCTAGCAGGCCAGCAACACAGCCTCTAAGTTAGAGCGGG  
 901 -----+-----+-----+-----+-----+ 960  
 CAGTGTCTCTCGGCTTAGTCCGATCGTCCGGGTCGTTGTGTCTGGAGATTCAATCTCGCCC  
 H K K P N Q P S R P S N T A S K L E R D -  
 ATAGTAACGCTGACAGAGAGACTATCAACCTGAAGGAACTTGAACCCCAAATTGCTTCAG  
 961 -----+-----+-----+-----+-----+ 1020  
 TATCATTGCGACTGTCTCTCTGATAGTTGGACTTCCCTTGAACCTTGGGGTTTAACGAAGTC  
 S N A D R E T I N L K E L E P Q I A S A -  
 CAAAACCAAATGCAGAGTGAAGGCAGTGAGAGCCTGAGGAAAGAGTTAAAAATTGCTTTG  
 1021 -----+-----+-----+-----+-----+ 1080  
 GTTTTGGTTTACGTCTCACTTCCGTCACCTCTCGGACTCCTTTCTCAATTTTAAACGAAAC  
 K P N A E \*  
 CCTGAAATAAGAAGTGCAGAGTTTCTCAGAATTCAAAAATGTTCTCAGCTGATTGGAATT  
 1081 -----+-----+-----+-----+-----+ 1140  
 GGACTTTATTCTTCACGTCTCAAAGAGTCTTAAGTTTTTACAAGAGTCGACTAACCTTAA  
 CTACAGTTGAATAATTAAAGAAC  
 1141 -----+-----+----- 1163  
 GATGTCAACTTATTAATTTCTTG

FIGURE 14 B



**B.CTLA4 Competition on hB7.2**  
**Competitors: hB7.1,hB7.2,hB7.2V,hB7.2C**

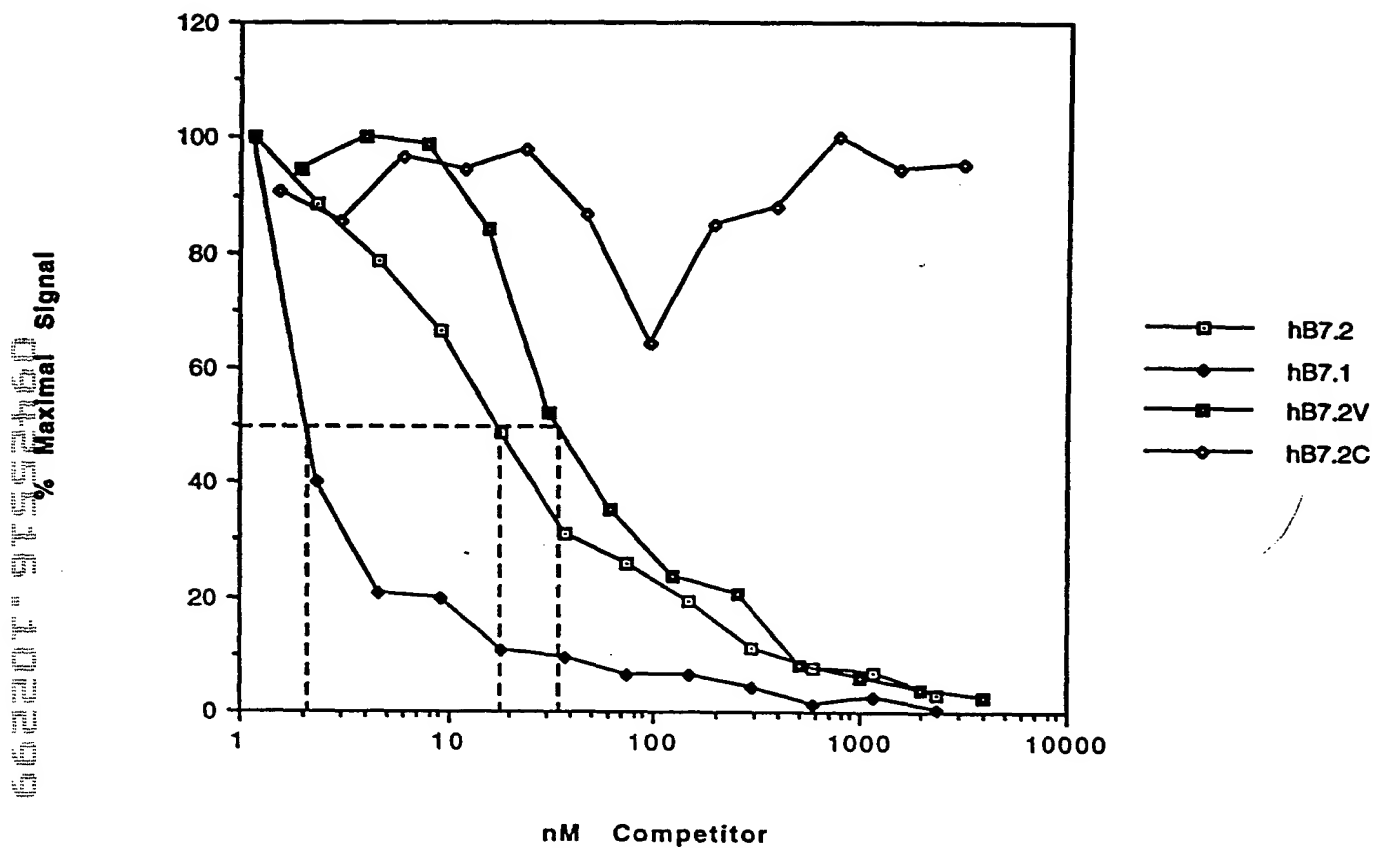


FIG. 15

0455460

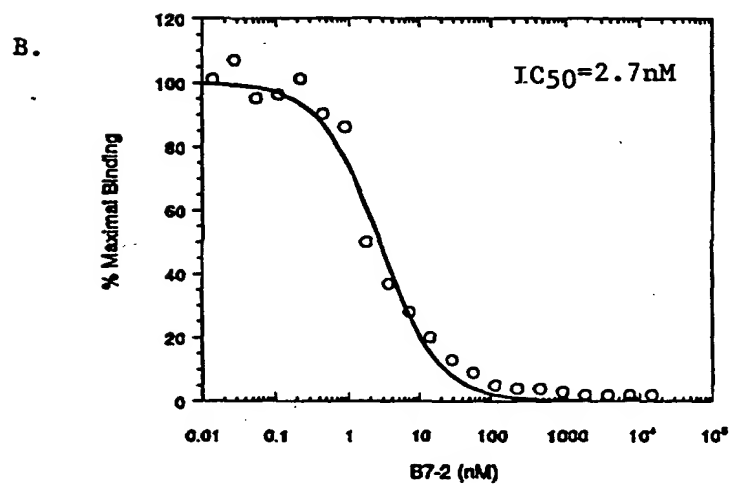
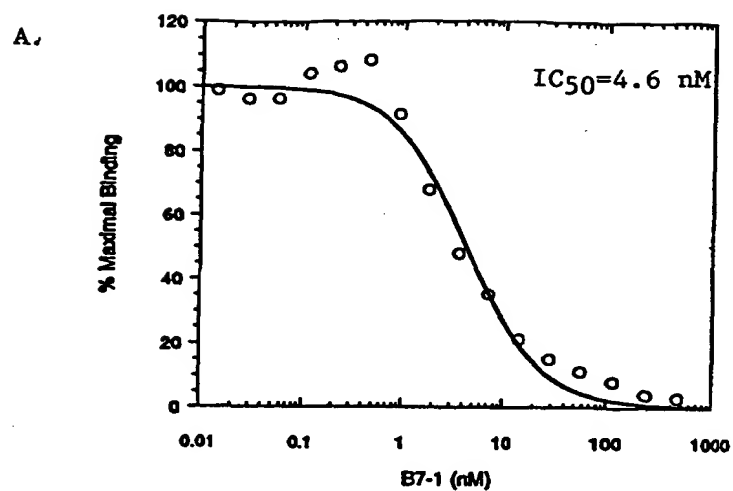
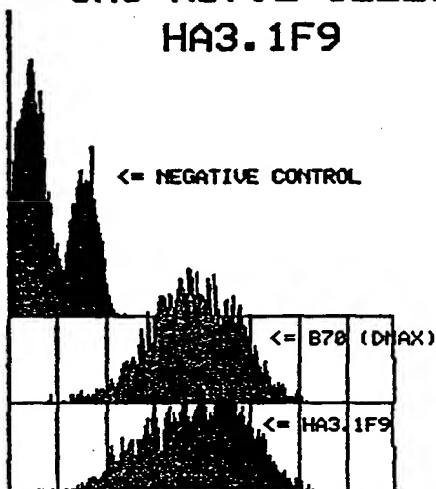


FIG. 16

#11:/23/HAHF003~FL1-H~FL1-Height

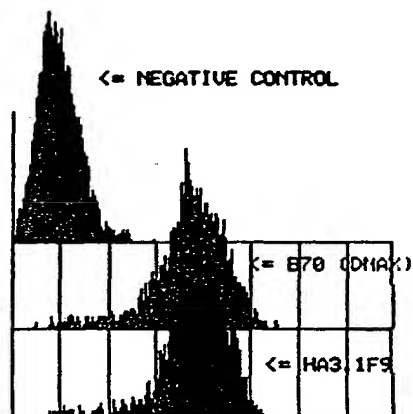
CHO-HB7.2 CELLS  
HA3.1F9



#11:/23/HAHF020~FL1-H~FL1-Height

3T3-HB7.2 CELLS  
HA3.1F9

B.



#11:/23/HAHF037~FL1-H~FL1-Height

3T3-NEO CELLS  
HA3.1F9

C.

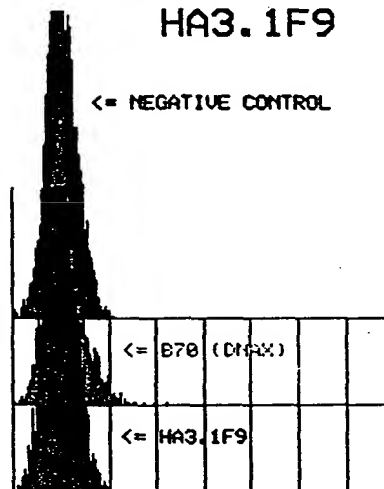
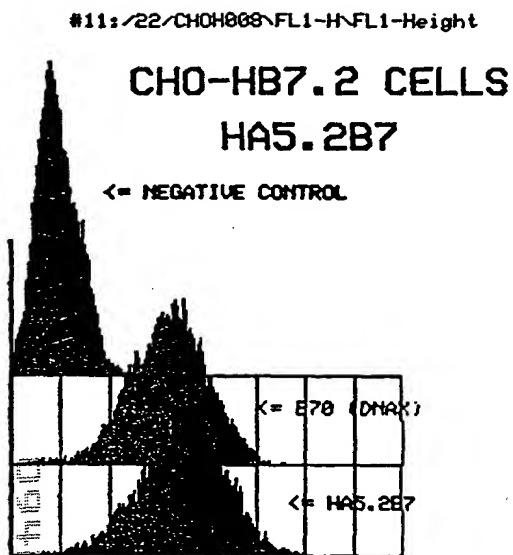
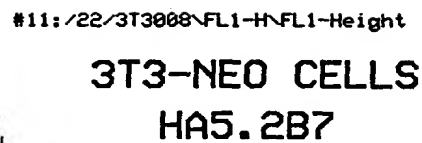
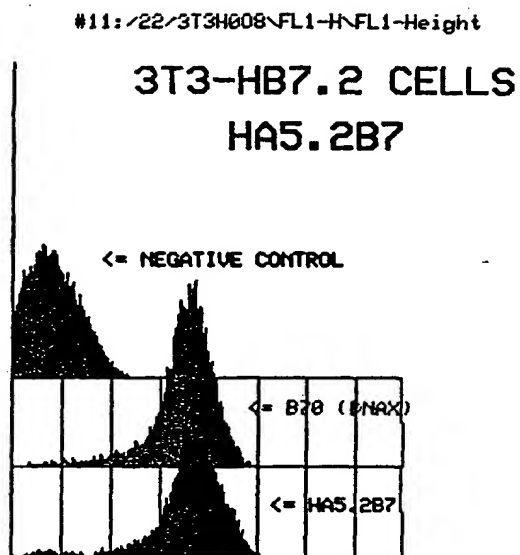


FIG. 17



B



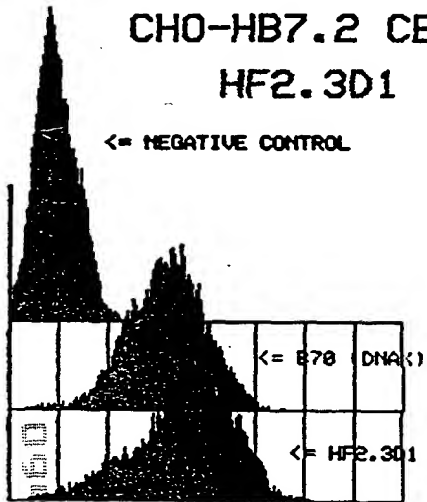
C

FIG. 18

#11:/22/CHOH003\FL1-H\FL1-Height

CHO-HB7.2 CELLS  
HF2.3D1

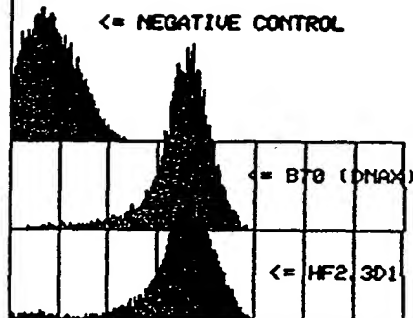
<= NEGATIVE CONTROL



#11:/22/3T3H003\FL1-H\FL1-Height

3T3-HB7.2 CELLS  
HF2.3D1

<= NEGATIVE CONTROL



#11:/22/3T3003\FL1-H\FL1-Height

3T3-NEO CELLS  
HF2.3D1

<= NEGATIVE CONTROL

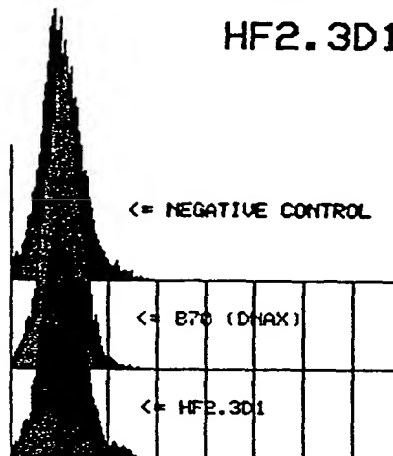


FIG. 19

# Binding of Modified Forms of B7 Family Members to CTLA4

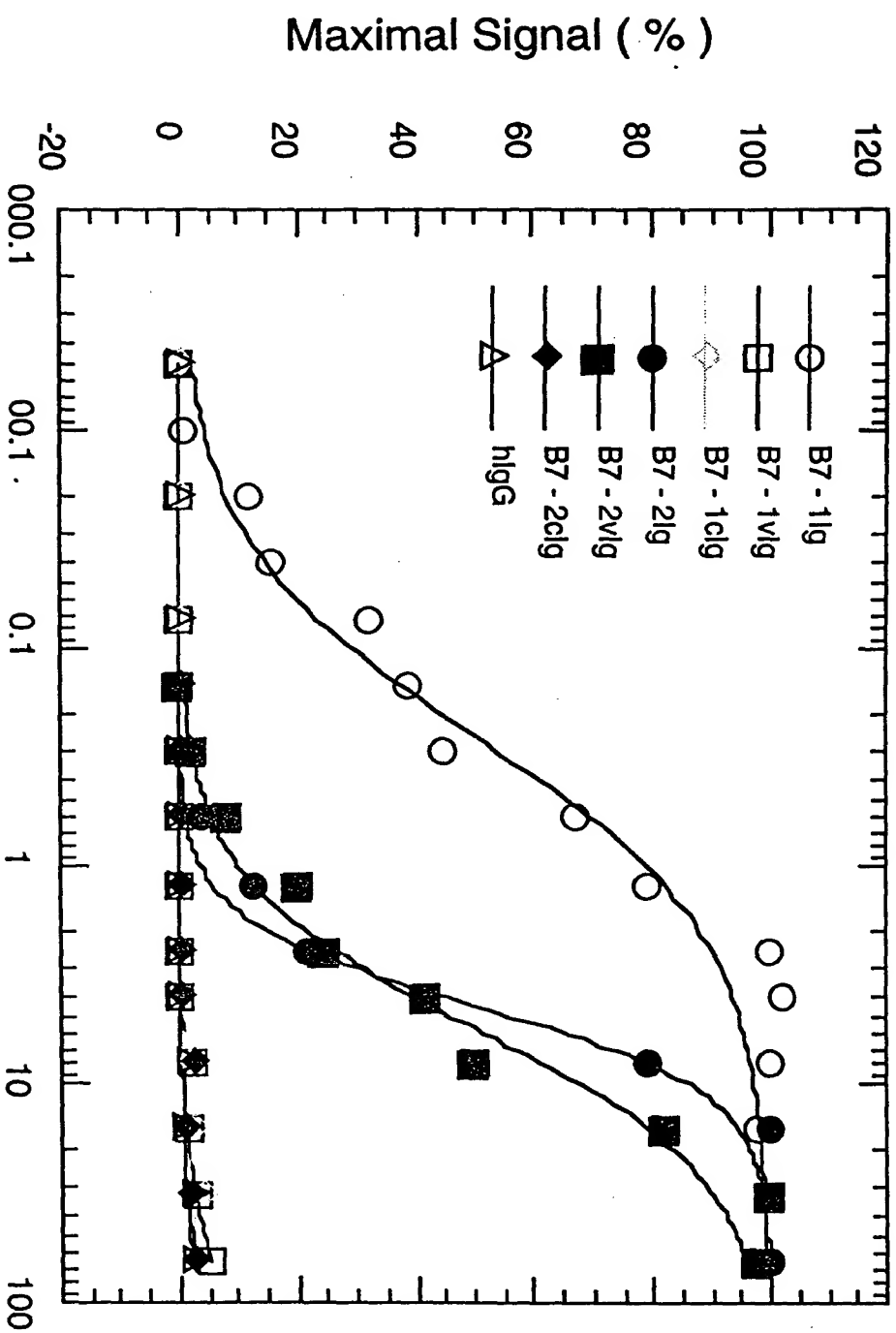


FIGURE 20

SELECTED PREFERENCES: Arithmetic/Lin ar

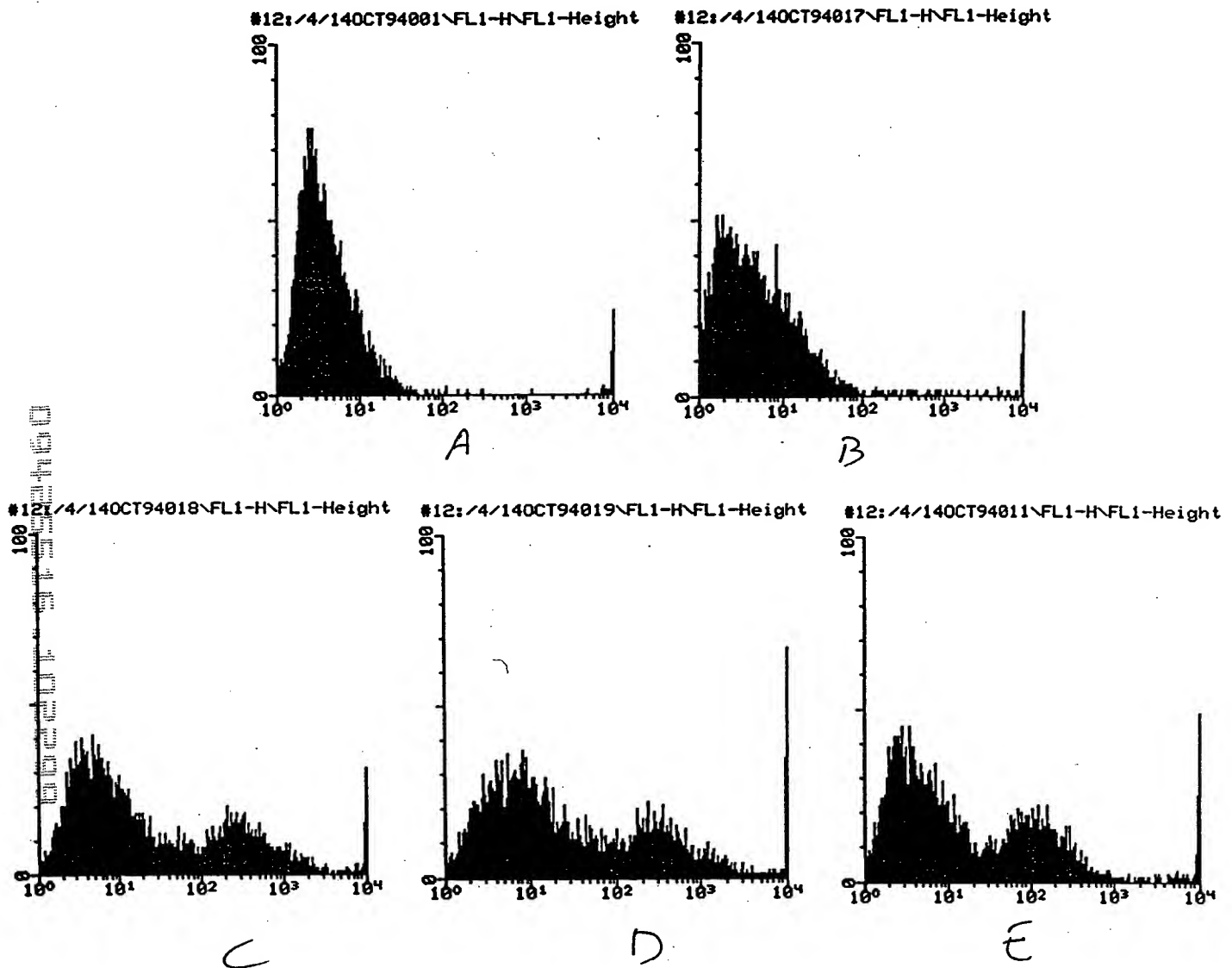


FIGURE 21

# FACS Analysis of CD28 + CHO Cells Using B7 Family Members

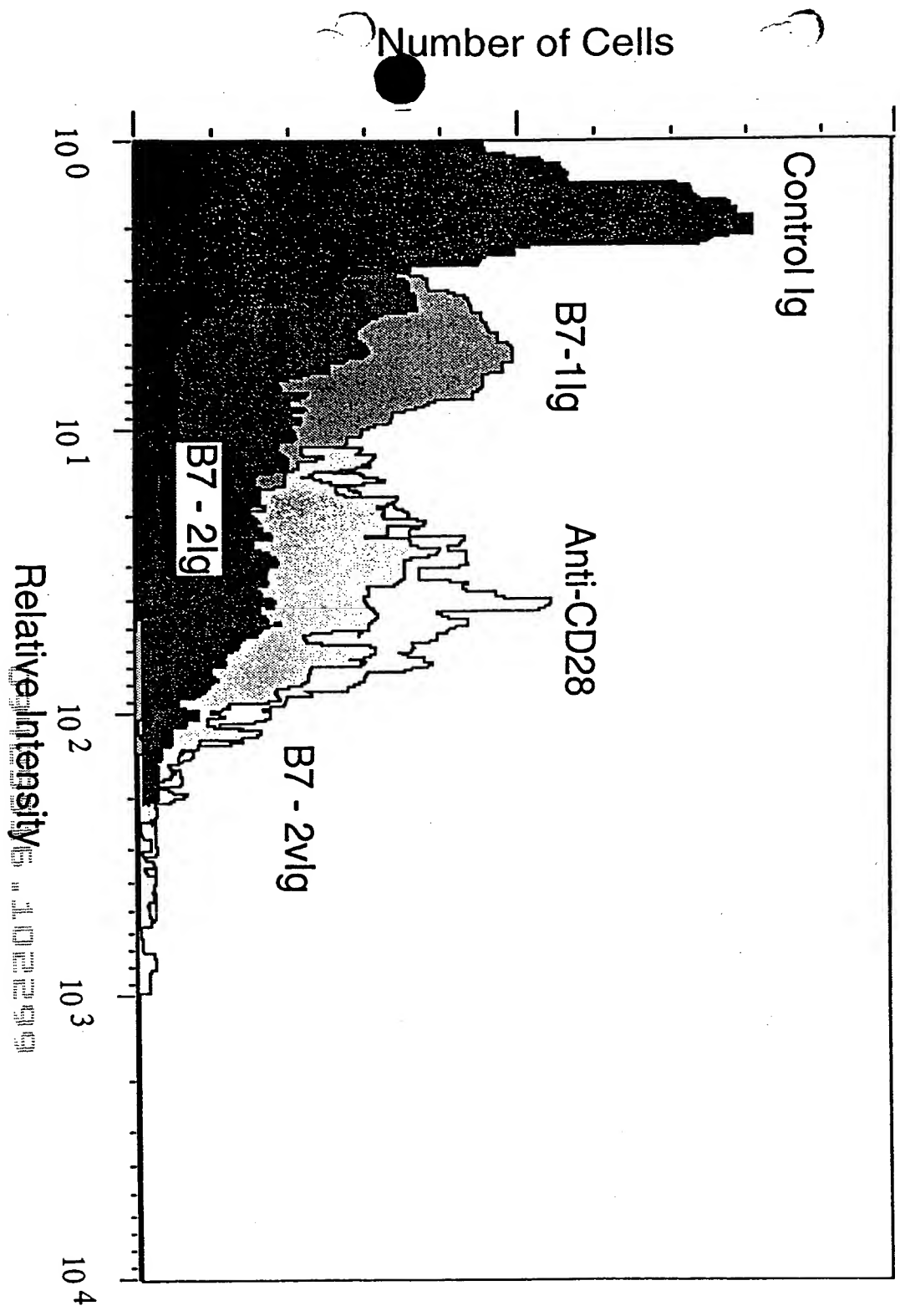


FIGURE 22



# The Variable Domain of B7-2 Can Provide a Costimulatory Signal for CD28 + T Cells

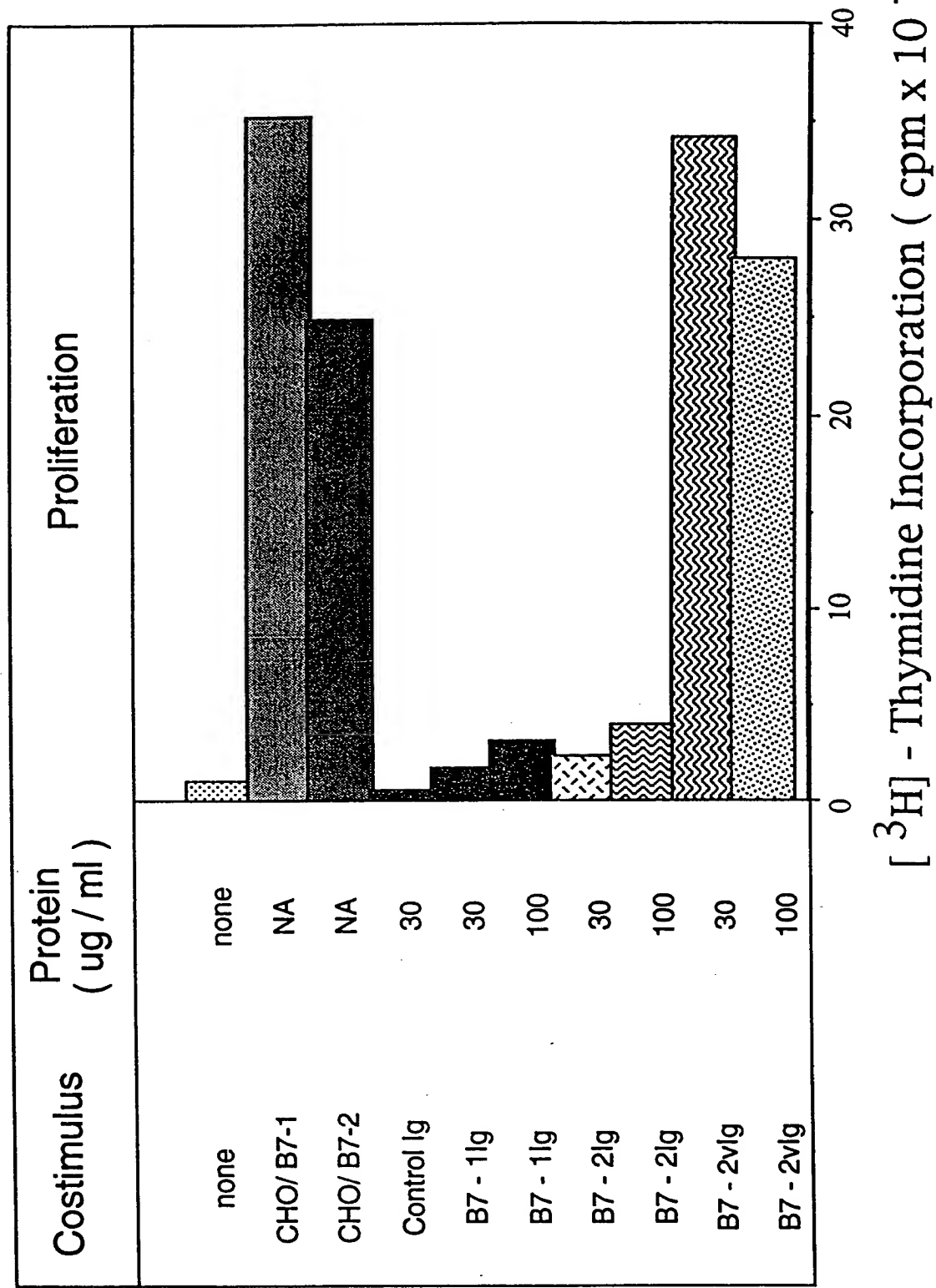


FIGURE 23

# Proliferation of CD28<sup>+</sup> T Cells to Costimulation by Soluble Proteins Prepared from B7 Family Members

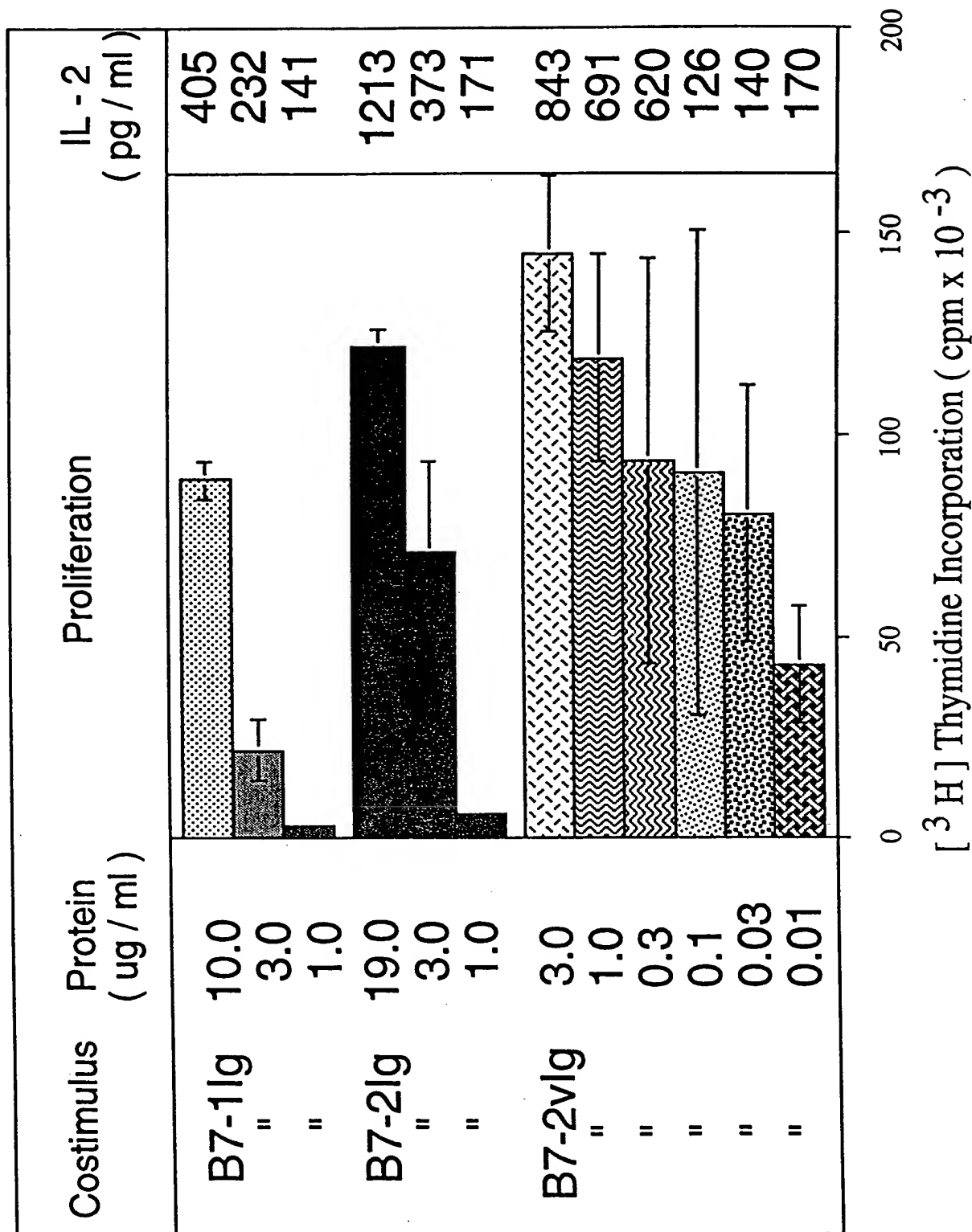


FIGURE 24

# Costimulation by B7-2vlg Induces Increased IL-2 Secretion

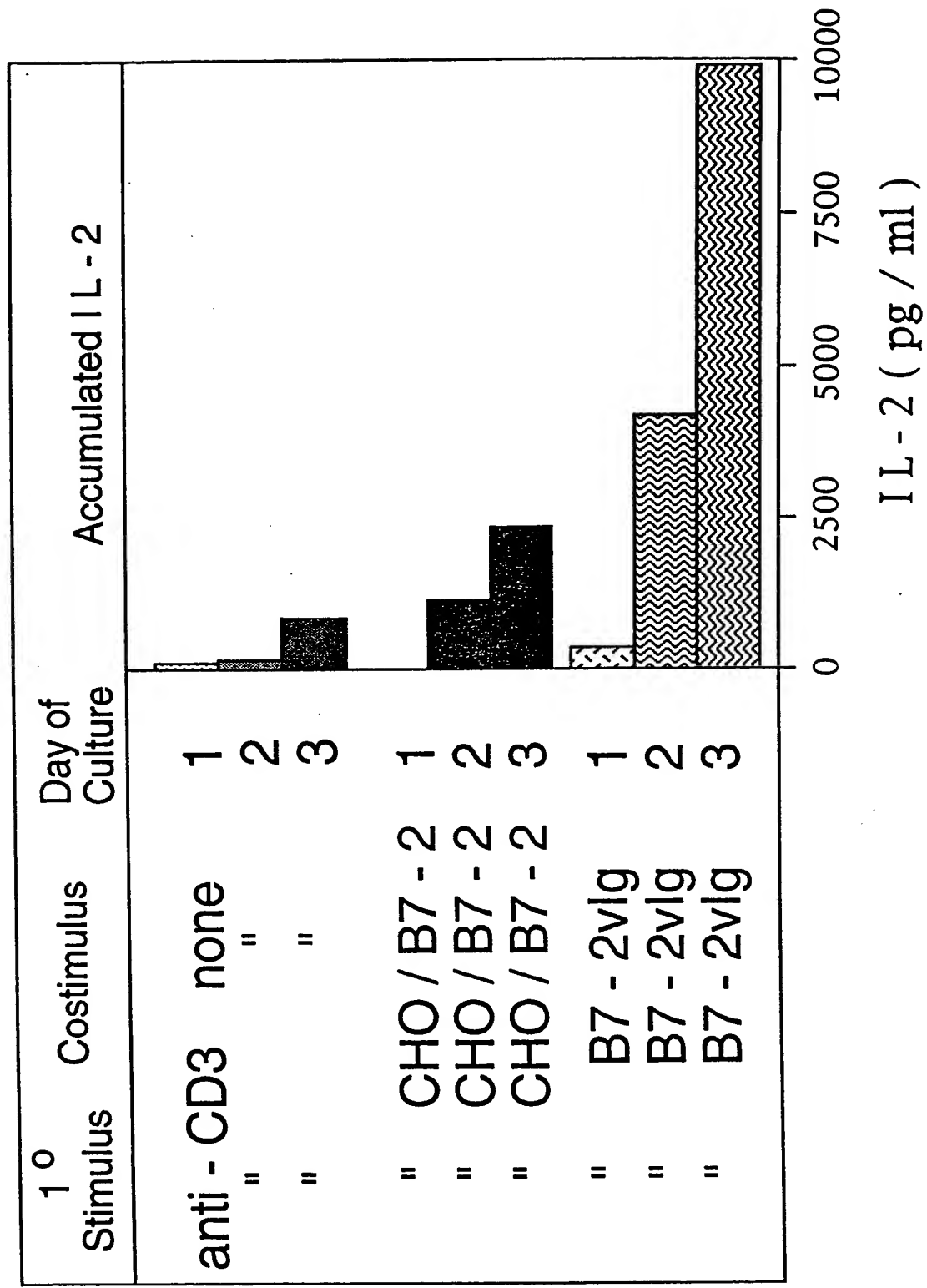


FIGURE 25

# Costimulation of T Cells by Soluble B7 Family Members Induces IL-2 Secretion

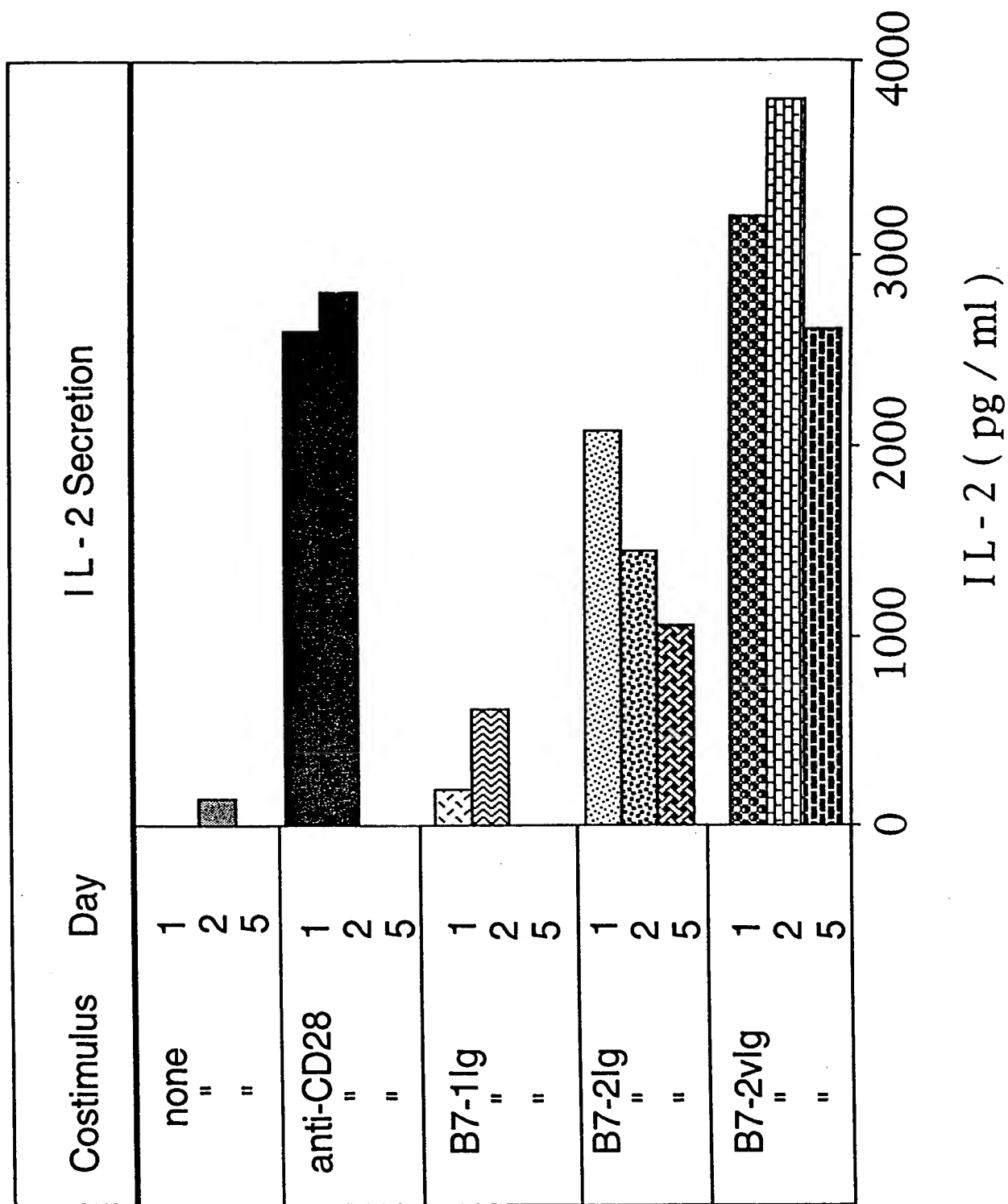


FIGURE 26

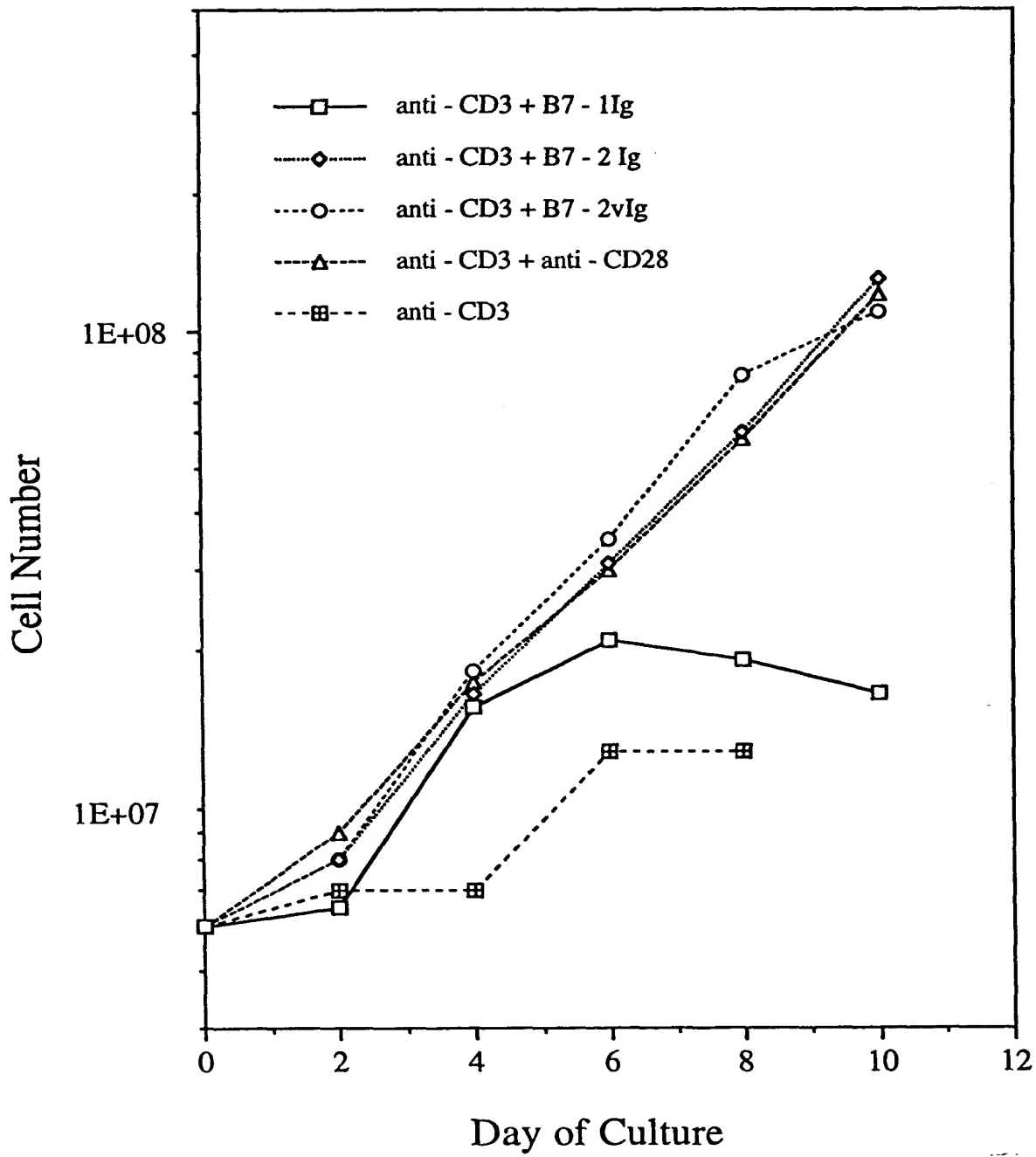


FIGURE 27